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NOTICE OF ALLOWANCE AND FEE(S) DUE

7590

12/16/2002

Jill A. Fahrlander Michael Best & Friedrich One South Pinckney Street P.O. Box 1806 Madison, WI 53701-1806

EX.	AMINER	
SOUAYA, JEHANNE E		
ART UNIT	CLASS-SUBCLASS	

DATE MAILED: 12/16/2002

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,338	03/29/2000	Steven Albert Benner	13238.9USC1	6192

TITLE OF INVENTION: METHODS FOR PREPARING OLIGONUCLEOTIDES CONTAINING NON-STANDARD NUCLEOTIDES

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$640	\$0	\$640	03/17/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. <u>PROSECUTION ON THE MERITS IS CLOSED.</u> THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

 Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.



PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Box ISSUE FEE Commissioner for Patents Washington, D.C. 20231
Fax (703)746-4000

appropriate. All further con	respondence including the selow or directed otherwis	Patent advance orders	and notification of	f maintenance fe	required). Blocks 1 through 4 sees will be mailed to the current ress; and/or (b) indicating a sep	correctionadance address as
	E ADDRESS (Note: Legibly mark- 90 12/16/2002	up with any corrections or use l	Block I)	ree(s) Transmi	ate of mailing can only be used for ttal. This certificate cannot papers. Each additional paper, s must have its own certificate of r	be used for any other such as an assignment or
Michael Best & Fri One South Pinckne P.O. Box 1806 Madison, WI 53701	y Street		_	United States Po envelope address	Certificate of Mailing or Tran that this Fee(s) Transmittal is stal Service with sufficient posta sed to the Box Issue Fee address e USPTO, on the date indicated b	being deposited with the ge for first class mail in an above, or being facsimile
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APPLN. TYPE nonprovisional	SMALL ENTITY YES	ISSUE FEE \$640	PUBLIC	ATION FEE	TOTAL FEE(S) DUE \$640	DATE DUE 03/17/2003
EXAMIN	IER	ART UNIT	CLASS-SUBCLA	ss		
SOUAYA, JEI	HANNE E	1634	514-100000			
1. Change of correspondence CFR 1.363). Change of corresponde Address form PTO/SB/12	nce address (or Change of	`	2. For printing of the names of up or agents OR, a single firm (hav	to 3 registered places to 3 registered places to 10 to	the name of a	
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3. ASSIGNEE NAME AND PLEASE NOTE: Unless at been previously submitted to (A) NAME OF ASSIGNEE	n assignee is identified beloto the USPTO or is being s	ow, no assignee data wi ubmitted under separate	**	tent. Inclusion of of this form is N	f assignee data is only appropriat OT a substitute for filing an assig COUNTRY)	e when an assignment has nment.
Please check the appropriate	assignee category or category	ories (will not be printed	on the patent)	☐ individual	□ corporation or other private gr	roup entity government
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(Authorized Signature)		(Date)				
NOTE; The Issue Fee and other than the applicant; a interest as shown by the rec	registered attorney or ag ords of the United States P	ent; or the assignee o atent and Trademark Of	r other party in			
This collection of informat obtain or retain a benefit be application. Confidentiality estimated to take 12 minute completed application form case. Any comments on its suggestions for reducing the Patent and Trademark Offin NOT SEND FEES OR Commissioner for Patents, Under the Paperwork Page.	COMPLETED FORMS Washington, DC 20231.	TO THIS ADDRES	S. SEND TO:			
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7	590 12/16/2002		EXAMINI	ER
Jill A. Fahrlande	r		SOUAYA, JEH	IANNE E
Michael Best & Fr One South Pinckno		ART UNIT	PAPER NUMBER	
P.O. Box 1806 Madison, WI 5370	11-1806		1634	
UNITED STATES		DATE MAILED: 12/16/2002		

Determination of Patent Term Extension under 35 U.S.C. 154 (b) (application filed after June 7, 1995 but prior to May 29, 2000)

The patent term extension is 0 days. Any patent to issue from the above identified application will include an indication of the 0 day extension on the front page.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (http://pair.uspto.gov)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.



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Michael Best & Fr	iedrich	-		
One South Pinckne	ey Street		ART UNIT	PAPER NUMBER
P.O. Box 1806			1634	
Madison, WI 5370	1-1806		1034	
UNITED STATES	}	I	DATE MAILED: 12/16/2002	

Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003; Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: http://www.uspto.gov/main/howtofees.htm.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Notice of Allowability

Application No. **09/538,338**

Applicant(s)

Steven Benner

Examiner

Jehanne Souaya

Art Unit **1634**



--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308. 1. X This communication is responsive to the proposed amendment filed 12/4/2002 2. X The allowed claim(s) is/are 6 and 12-14 3. The drawings filed on are accepted by the Examiner. 4. Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d). a) 🗌 All b) Some* c) None of the: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. 3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)). *Certified copies not received: 5. Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application). (a) The translation of the foreign language provisional application has been received. 6. X Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121. Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE. 7. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient. 8. X CORRECTED DRAWINGS must be submitted. (a) I including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached 1) \boxtimes hereto or 2) \square to Paper No. . (b) \sqcup including changes required by the proposed drawing correction filed approved by the examiner. (c) including changes required by the attached Examiner's Amendment/Comment or in the Office action of Paper No. Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson. 9. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL. Attachment(s) 1 Notice of References Cited (PTO-892) 2 Notice of Informal Patent Application (PTO-152) 4 X Interview Summary (PTO-413), Paper No. 17. 3 X Notice of Draftsperson's Patent Drawing Review (PTO-948) 5 Information Disclosure Statement(s) (PTO-1449), Paper No(s). 6 X Examiner's Amendment/Comment 7 Examiner's Comment Regarding Requirement for Deposit of Biological 8 X Examiner's Statement of Reasons for Allowance Material 9 Other

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EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jill Fahrlander on 12/11/2002.

- 2. The application has been amended as follows:
- In claim 12, line 15, delete the recitation of "comprises" and insert instead -- is performed with--.
 - In claim 12, line 15, delete the recitation of "DNA".
- In claim 12, line 16, delete the recitation of "T4 DNA polymerase,".
- In claim 13, line 1, delete the recitation of "DNA".
- ✓ In claim 13, line 1, delete the recitation of "comprises" and insert instead --is--.
- In claim 14, line 16, delete the recitation of "comprises" and insert instead -- is performed with--.

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REASONS FOR ALLOWANCE

3. The following is an examiner's statement of reasons for allowance: The claims are drawn to a method of making an oligonucleotide comprising a template oligonucleotide comprising a sequence of nucleotides wherein the template comprises at least one non standard nucleotide at a preselected site in the sequence, wherein the non standard nucleotide is iso-G or iso-C; contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides in the template, wherein the nucleotide triphosphate complementary to the non standard nucleotide at the preselected site comprises a derivatized nucleotide; and forming an oligonucleotide complementary to a portion of the template by enzymatic polymerization of the nucleotides triphosphates in a sequence complementary to a portion of the template. The claims are also drawn to a method of making an oligonucleotide comprising a template oligonucleotide comprising a sequence of nucleotides wherein the template comprises at least one non standard nucleotide at a preselected site in the sequence; contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides in the template, wherein the nucleotide triphosphate complementary to the non standard nucleotide at the preselected site comprises a derivatized nucleotide; and forming an oligonucleotide complementary to a portion of the template by enzymatic polymerization of the nucleotide triphosphates in a sequence complementary to a portion of the template, wherein the enzymatic polymerization is performed with AMV reverse transcriptase or Klenow Fragment of DNA

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polymerase I. The claims are further drawn to a method of making an oligonucleotide comprising a template oligonucleotide comprising a sequence of nucleotides wherein the template comprises at least one non standard nucleotide at a preselected site in the sequence; contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides in the template, wherein the nucleotide triphosphate complementary to the non standard nucleotide at the preselected site comprises a derivatized nucleotide comprising radiolabel; and forming an oligonucleotide complementary to a portion of the template by enzymatic polymerization of the nucleotides triphosphates in a sequence complementary to a portion of the template, wherein the enzymatic polymerization is performed with T7 RNA polymerase.

The closest prior art is that of Eritja et al., (Nucleic Acids Research, 1986; 14(20), pp 8135-8153) which teaches a method for making an oligonucleotide using a template containing xanthine and contacting the template with a mixture of nucleotide triphosphates including 9-(β--D-2'-deoxyribofuranosyl)-2-aminopurine triphosphate (dAPTP) and Drosophila polymerase α to form an oligonucleotide complementary to the template (dATPT is also incorporated in the oligonucleotide opposite xanthine in the template). The claims are allowable over the prior art of Eritja et al because Eritja et al do not teach using iso-G or iso-C either in the template or as a derivatized nucleotide triphosphate, nor does Eritja teach forming an oligonucleotide with Klenow fragment of DNA polymerase I, AMV reverse transcriptase or T7 RNA polymerase. Eritja et al teach away from using Klenow fragment because Eritja et al teach that when Klenow

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fragment was used as the polymerase, which has 3' exonuclease activity, removal of the nucleotide opposite xanthine and extensive degradation of the primer was observed (p. 8142, last para). Therefore, Eritja et al does not teach a reasonable explanation of success that any polymerase, such as T7 RNA polymerase, Klenow fragment of DNA polymerase I (which the specification teaches were successful in the instantly claimed methods), or AMV reverse transcriptase would be capable of use in the method of Eritja et al.

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya Patent examiner Art Unit 1634

JEHANNE SOUAYA
PATENT EXAMINER

Icharne Sovaya 12/12/02